PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference TSRI-651.6PC	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/37653	International filing date *(day/month/year)* 18 November 2003 (18.11.2003)	Priority date *(day/month/year)* 18 November 2002 (18.11.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): A61K 31/519, 38/45 and US Cl.: 514/262.1; 424/94.5		
Applicant THE SCRIPPS RESEARCH INSTITUTE		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand 18 June 2004 (18.06.2004)	Date of completion of this report 25 July 2005 (25.07.2005)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Rebecca E. Prouty Telephone No. 571-272-1600

Form PCT/IPEA/409 (cover sheet)(July 1998)

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International application No.
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I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-35 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 36-39, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-20, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the sequence listing part of the description:
pages 1-10, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☒ contained in the international application in printed form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 7-9,18-20,28,32 and 33

because:

☐ the said international application, or the said claim Nos. ____ relate to the following subject matter which does not require international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. ____ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 7-9,18-20,28,32 and 33

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

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V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims 6, 12, 13, 17, 27, 31	YES
	Claims 1-5, 10, 11, 14-16, 21-26, 29, 30	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-6, 10-17, 21-27, 29-31	NO
Industrial Applicability (IA)	Claims 1-6, 10-17, 21-27, 29-31	YES
	Claims NONE	NO

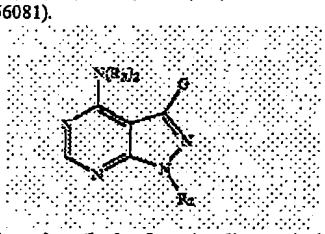
2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1-5, 10, 11, 14-16, 21-25, 29, and 30 lack novelty under PCT Article 33(2) as being anticipated by Feng et al. (US Patent 5,731,343).

Feng et al. teach methods of treating diseases including myocardial infarction using with the compound radicicol (see column 2, lines 37-41 and column 3, lines 54-60). Radicicol is disclosed as an inhibitor of the tyrosine kinase Src (see example 2). Feng et al. further teach that radicicol can be administered by intraperitoneal injection, intravenous injection, orally or parentally (see column 7, lines 34-40). Thus Feng et al. anticipate all of the instant claims.

Claims 1-5, 10, 11, 14-16, 21-26, 29, and 30 lack novelty under PCT Article 33(2) as being anticipated by Hirst et al. (US-PGPUBS 2002/0156081).



Hirst et al. teach methods of treating diseases including myocardial infarction using tyrosine kinase inhibitors having the structure shown (see paragraph 313 and 364). These compounds are disclosed as inhibitors of tyrosine kinases including Src kinases (see paragraphs 311 and 349). Hirst et al. further teach that these compounds can be administered by intraperitoneal injection, intravenous injection, orally or parentally (see paragraph 391) Thus Hirst et al. anticipate all of the instant claims.

Claims 1-4, 11, 14, 15, 21-25, and 29 lack novelty under PCT Article 33(2) as being anticipated by Das et al. (US-PGPUBS 2002/0123484).

Das et al. teach methods of treating diseases including myocardial infarction using tyrosine kinase inhibitors (see paragraph [0164]). These compounds are disclosed as inhibitors of tyrosine kinases including Src kinases (see paragraph [0161]). Das et al. further teach that these compounds can be administered by intravenous injection, orally or parentally (see paragraph [0170]). Thus Das et al. anticipate all of the instant claims.

Claims 1-4, 11, 14, 15, 21-25, and 29 lack novelty under PCT Article 33(2) as being anticipated by Barrish et al. (US Patent 6,235,740).

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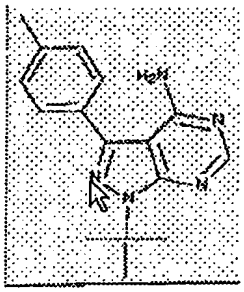
Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Barrish et al. teach methods of treating diseases including myocardial infarction using tyrosine kinase inhibitors (see column 17, line 66 - column 18, line 6). These compounds are disclosed as inhibitors of tyrosine kinases including Src kinases (see column 17, lines 34-36). Barrish et al. further teach that these compounds can be administered by intravenous injection, orally or parentally (see column 19, lines 33-38). Thus Barrish et al. anticipate all of the instant claims.

Claims 6, 12, 13, 17, 27, and 31 lack an inventive step under PCT Article 33(3) as being obvious over Hirst et al. (US-PGPUBS 2002/0156081) in view of Hanke et al.

Hirst et al. is discussed above and teaches the treatment of myocardial infarction with tyrosine kinase inhibitors which inhibit tyrosine kinases including Src kinases. Hirst et al. does not specifically teach the use of the pyrazolopyrimidine PP1 (also called AGL 1872) for the treatment of myocardial infarction. Hanke et al. teach the pyrazolopyrimidine PP1 having the structure shown below.



Hanke teach that PP1 is a tyrosine kinase inhibitor which inhibits Src kinases. Hanke et al. do not teach the use of PP1 or PP2 to treat myocardial infarction.

The structural similarity of PP1 to the tyrosine kinase inhibitor of Hirst et al. is readily apparent to a skilled artisan and these compounds are similarly disclosed as tyrosine kinase inhibitors which inhibit tyrosine kinases including Src kinases. As such it would have been obvious to one of skill in the art to use PP1 to treat myocardial infarction as taught Hirst et al. for the structurally and functionally similar tyrosine kinase inhibitors. Furthermore, as it is well known in the art that treatment of myocardial infarction is most successful when treated as soon after the infarction, it would have been obvious to one of skill in the art to administer the inhibitor within the first 6 hours after the infarction.